

WHAT IS CLAIMED IS:

1. A method for directly delivering a substance into an intradermal space within a mammal, the method comprising bolus administration of said substance into the dermis, whereby the administered substance has at least one improved pharmacokinetic parameter relative to the same pharmacokinetic parameter produced upon administration of the same substance subcutaneously.

2. The method of claim 1 wherein the administering is through at least one small gauge hollow needle.

3. The method of claim 1 wherein the needle has an outlet with an exposed height between 0 and 1 mm.

4. The method of Claim 1 wherein administering comprises inserting the needle to a depth which delivers the substance at least about 0.3 mm below the surface to no more than about 2 mm below the surface.

5. The method of Claim 4 wherein administering comprises inserting the needle into the skin to a depth of at least about 0.3 mm and no more than about 2 mm.

6. The method of claim 1 wherein the improved pharmacokinetics is a decrease in T_{max} .

7. The method of claim 1 wherein the improved pharmacokinetics is an increase in C_{max} .

8. The method of claim 1 wherein the improved pharmacokinetics is a decrease in T_{lag} .

10028988-122801

9. The method of claim 1 wherein the improved pharmacokinetics is an enhanced absorption rate.

10. The method of claim 1 wherein the substance is administered over a time period of not more than ten minutes.

11. The method of claim 1 wherein the substance is administered at a rate between 1 nL/min. and 200 mL/min.

12. The method of claim 1 wherein said substance is a hormone.

13. The method of claim 12 wherein the hormone is a growth hormone.

14. The method of claim 13 wherein the growth hormone is human growth hormone.

15. The method of claim 1 wherein the substance has a molecular weight greater than 1000 daltons.

16. The method of claim 1 wherein said substance is hydrophobic.

17. The method of claim 1 wherein said substance is hydrophilic.

18. The method of claim 1 wherein the needle(s) are inserted substantially perpendicularly to the skin.

19. A method of administering a pharmaceutical substance comprising administering the substance intradermally through one or more microneedles having a length and outlet suitable for selectively delivering the substance into the dermis over a time period of not more than ten minutes to obtain absorption of the substance in the

*

dermis thereby producing improved systemic pharmacokinetics compared to subcutaneous administration.

20. The method of Claim 19 wherein the improved pharmacokinetics is decreased T_{\max} .

21. The method of claim 19 wherein the improved pharmacokinetics is an increase in C_{\max} .

22. The method of claim 19 wherein the improved pharmacokinetics is a decrease in T_{lag} .

23. The method of claim 19 wherein the improved pharmacokinetics is an enhanced absorption rate.

24. The method of claim 19 wherein the length of the microneedle is from about 0.3 mm to about 2.0 mm.

25. The method of Claim 19 wherein the microneedle is a 30 to 50 gauge needle.

26. The method of Claim 19 wherein the microneedle has an outlet of from 0 to 1 mm.

27. The method of Claim 19 wherein the microneedle is configured in a delivery device which positions the microneedle substantially perpendicular to skin surface.

28. The method of Claim 19 wherein the microneedle needle is contained in an array of microneedles.

29. The method of Claim 28 wherein the array comprises 3 microneedles.

30. The method of Claim 28 wherein the array comprises 6 microneedles.

31. A method for administering a macromolecular and/or hydrophobic pharmaceutical substance to a patient, the method comprising selective bolus delivery of the substance intradermally to achieve a substantially higher C_{max} and/or a substantially shorter T_{max} and/or a substantially shorter time to reach a threshold blood serum concentration for pharmaceutical effect of the substance, by comparison with subcutaneous administration of the substance at an identical dose and rate of delivery.



32. The method of claim 31 wherein selectively delivering the substance intradermally comprises selectively injecting the substance intradermally.

33. The method of claim 31 wherein administering comprises infusing the substance over a period of from about 2 min to about 10 min.

34. The method of claim 31 wherein administering comprises delivering a bolus of the substance over a period of less than 10 minutes.

35. The method of claim 31 wherein administering the substance intradermally comprises administering the substance through a needle having a length and outlet configuration which allows selective intradermal delivery of the substance.

36. The method of claim 35 wherein the microneedle has a length of from about 0.3 mm to about 2.0 mm.

37. The method of claim 35 wherein the microneedle is a 30 to 50 gauge needle.

38. The method of Claim 35 wherein the microneedle is configured in a delivery device which positions the microneedle substantially perpendicular to skin surface.

39. The method of Claim 35 wherein the microneedle needle is in an array of microneedles.

40. The method of Claim 39 wherein the array comprises 3 microneedles.

41. The method of Claim 39 wherein the array comprises 6 microneedles.

42. The method of claim 31 wherein the substance is administered at a volume rate of from about 2 microliters per minute to about 200 milliliters per minute.

43. The method of claim 42 wherein the substance is administered at a volume rate of from about 2 microliters per minute to about 10 milliliters per minute.

44. The method of claim 42 wherein the substance is administered at a volume rate of from about 10 microliters per minute to about 200 milliliters per minute.

45. The method of claim 31 wherein the substance comprises a polysaccharide.

46. The method of claim 31 wherein the substance comprises heparin molecule or a fragment thereof having anticoagulant activity.

47. The method of claim 31 wherein the substance comprises Fragmin®.

48. The method of claim 31 wherein the substance comprises a protein.

49. The method of claim 31 wherein the protein comprises a human growth hormone.

50. The method of claim 31 wherein the substance comprises Genotropin®.

51. The method of claim 42 wherein the rate is constant, variable or combinations thereof.

52. The method of claim 31 wherein the substance comprises a pegylated protein.

53. A method for delivering a bioactive substance to a subject comprising: contacting the skin of the subject with a device having a dermal-access means for accurately targeting the dermal space of the subject with an efficacious amount of the bioactive substance and administering a bolus of the substance into the dermis, wherein the pharmacokinetics of the bioactive substance is improved relative to the pharmacokinetics of the substance when administered subcutaneously.

54. The method of claim 53 wherein the improved pharmacokinetics is a decrease in T_{\max} .

55. The method of claim 53 wherein the improved pharmacokinetics comprises an increase in C_{\max} of the substance compared to subcutaneous injection.

56. The method of claim 53 wherein the improved pharmacokinetics is a decrease in T_{lag} .

57. The method of Claim 53 wherein the device has a fluid driving means including a syringe, infusion pump, piezoelectric pump, electromotive pump, electromagnetic pump, or Belleville spring.

58. The method of Claim 53 wherein the dermal access means comprises one or more hollow microcannula having a length of from about 0.3 to about 2.0mm.

59. The method of Claim 53 wherein said dermal access means comprises one or more hollow microcannula having an outlet with an exposed height between 0 and 1 mm.

60. A method for delivering a bioactive substance to a subject comprising: contacting the skin of a subject with a device having a dermal-access means for accurately targeting the dermal space of the subject with an efficacious amount of the bioactive substance at a rate of 1nL/min. to 200 mL/ min. and delivering the substance into the dermis over a time period of not more than ten minutes; wherein the rapid onset pharmacokinetics of the bioactive substance is substantially improved relative to subcutaneous injection.



61. The method of claim 60 wherein the pharmokinetics is a decreased T_{max} .

62. The method of claim 60 wherein the pharmokinetics is an increased C_{max} .

63. The method of claim 60 wherein the pharmokinetics is a decreased T_{lag} .

64. The method of claim 60 wherein the pharmokinetics is an enhanced absorption rate.

65. The method of claim 60 wherein the dermal access means has one or more hollow microcannula that inserts into the skin of said subject to a depth of from about 0.3 to about-2.0 mm.

66. The method of claim 60 wherein the dermal access means has one or more hollow microcannula having an outlet with an exposed height between 0 and 1 mm.